

CLAIMS

1. A light chain (L chain) variable region (V region) of mouse monoclonal antibody to the human interleukin-6 receptor (IL-6R).

5 2. An L chain V region according to claim 1, having an amino acid sequence shown in any one of SEQ ID NOS: 24, 26, 28 and 30.

3. A heavy chain (H chain) V region of a mouse monoclonal antibody to the human IL-6R.

10 4. An H chain V region according to claim 3, having an amino acid sequence shown in SEQ ID NOS: 25, 27, 29 and 31.

5. A chimeric antibody to the human IL-6R, comprising:

15 (1) an L chain comprising a human L chain constant region (C region) and an L chain V region of a mouse monoclonal antibody to the human IL-6R; and

20 (2) an H chain comprising a human H chain C region and an H chain V region of a mouse monoclonal antibody to the human IL-6R.

25 6. A chimeric antibody according to claim 5, wherein the mouse L chain V region has an amino acid sequence shown in any one of SEQ ID NOS: 24, 26, 28 and 30; and the mouse H chain V region has an amino acid sequence shown in any one of SEQ ID NOS: 25, 27, 29 and 31.

30 7. Complementarity determining regions (CDRs) of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

8. CDR according to claim 7, having amino acid sequence shown in any one of SEQ ID NOS: 24, 26, 28 and 30 wherein the stretch of the amino acid sequence is defined in Table 9.

35 9. CDR of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

10. CDR according to claim 9, having amino acid sequence shown in any one of SEQ ID NOS: 25, 27, 29, and

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31 wherein the stretch of the amino acid sequence is defined in Table 9.

11. A reshaped human L chain V region of an antibody to the human IL-6R, comprising:

5 (1) framework regions (FRs) of a human L chain V region, and

(2) CDRs of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

10 12. A reshaped human L chain V region according to claim 11, wherein the CDRs have amino acid sequences shown in any one of SEQ ID Nos.: 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

15 13. A reshaped human L chain V region according to claim 11, wherein the FRs are derived from the human antibody REI.

14. A reshaped human L chain V region according to claim 11, having an amino acid sequence shown as RV_La or RV_Lb in Table 2.

20 15. A reshaped human L chain V region according to claim 11, having an amino acid sequence shown as RV_L in Table 5.

16. A reshaped human H chain V region of an antibody to the human IL-6R, comprising:

25 (1) FRs of a human H chain V region, and

(2) CDRs of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

30 17. A reshaped human H chain V region according to claim 16, wherein the CDRs have amino acid sequences shown in SEQ ID NOS: 25, 27, 29 and 31 wherein the stretches of the amino acid sequences are defined in Table 9.

35 18. A reshaped human H chain V region according to claim 16, wherein the FRs are derived from the human antibody NEW or HAX.

19. A reshaped human H chain V region according to

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claim 16, having an amino acid sequence shown in Table 3 as RV_Ha, RV_Hb, RV_Hc, RV_Hd, RV_He or RV_Hf.

20. A reshaped human H chain V region according to claim 17, having an amino acid sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 7.

5 21. An L chain of a reshaped human antibody to human IL-6R comprising:

(1) a human L chain C region; and

10 (2) an L chain V region comprising human L chain FRs and L chain CDRs of mouse monoclonal antibody to human IL-6R.

15 22. A reshaped human antibody L chain according to claim 21, wherein the human L chain C region is a human γ -1C region, the human L chain FRs are derived from REI, and the L chain CDRs have amino acid sequences shown in SEQ ID Nos. 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

20 23. A reshaped human antibody L chain according to claim 21, wherein the L chain V region has an amino acid sequence shown as RV_La or RV_Lb in Table 2.

24. A reshaped human antibody L chain according to claim 21, wherein the L chain V region has an amino acid sequence shown as RV_L in Table 5.

25 25. An H chain of a reshaped human antibody to human IL-6R comprising:

(1) a human H chain C region, and

30 (2) an H chain V region comprising human H chain FRs, and H chain CDRs of mouse monoclonal antibody to human IL-6.

35 26. A reshaped human antibody H chain according to claim 25, wherein the human H chain C region is human κ C region, the human H chain FRs are derived from NEW or HAX, the H chain CDRs have amino acid sequences shown in SEQ ID NOS: 25, 27, 29 or 31 wherein the stretches of the amino acid sequences are defined in Table 9.

27. A reshaped human antibody H chain according to

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claim 25, wherein the H chain V region has an amino acid sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 3.

28. A reshaped human antibody H chain according
claim 25, wherein the H chain V region has an amino acid
5 sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 6, or
RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 7.

29. A reshaped antibody to the human IL-6R,
comprising:

(A) an L chain comprising,

10 (1) a human L chain C region, and

(2) an L chain V region comprising human
L chain FRs, and L chain CDRs of a mouse monoclonal
antibody to the human IL-6R; and

(B) an H chain comprising,

15 (1) a human H chain C region, and

(2) an H chain V region comprising human
H chain FRs, and H chain CDRs of a mouse monoclonal
antibody to the human IL-6R.

30. A reshaped human antibody according to
20 claim 29, wherein the L chain CDRs have amino acid
sequences shown in any one of SEQ ID NOS: 24, 26, 28 and
30 wherein the stretches of the amino acid sequences are
defined in Table 9; the H chain CDRs have amino acid
sequence shown in any one of SEQ ID NOS: 25, 27, 29 and
25 31 wherein the stretches of the amino acid sequences are
defined in Table 9; the human L chain C region and human
L chain FRs are derived from the REI; and the human H
chain C region and human FRs are derived from the NEW or
HAX.

30. 31. A reshaped human antibody according to
claim 29, wherein the L chain V region has an amino acid
sequence shown as RV_La or RV_Lb in Table 2.

32. A reshaped human antibody according to
claim 29, wherein the L chain V region has an amino acid
35 sequence shown as RV_L in Table 5.

33. A reshaped human antibody according to

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claim 29, wherein the H chain V region has an amino acid sequence shown in Table 3 as RV_Ha, RV_Hb, RV_Hc, RV_Hd, RV_He or RV_Hf.

5 34. A reshaped human antibody according to
claim 29, wherein the H chain V region has an amino acid sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 6, or RV_Ha, RV_Hb, RV_Hd in Table 7.

10 35. A DNA coding for an L chain V region of a mouse monoclonal antibody to the human IL-6R.

15 36. A DNA according to claim 35, wherein the L chain V region has an amino acid sequence shown in any one of SEQ ID NOS: 24, 26, 28 and 30.

37. A DNA coding for an H chain V region of a mouse monoclonal antibody to the human IL-6R.

20 38. A DNA according to claim 37, wherein the H chain V region has an amino acid sequence shown in any one of SEQ ID NOS: 25, 27, 29 and 31.

39. A DNA coding for CDR of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

25 40. A DNA coding for CDR according to claim 39, wherein the CDR has an amino acid sequence in any one of SEQ ID NOS: 24, 26, 28 and 30 wherein the stretch of the amino acid sequence is defined in Table 9.

41. A DNA coding for CDR of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

25 42. A DNA coding for CDR according to claim 41, wherein the CDR has an amino acid sequence shown in any one of SEQ ID NOS: 25, 27, 29 and 31 wherein the stretch of the amino acid sequence is defined in Table 9.

30 43. A DNA coding for a reshaped human L chain V region of an antibody to the human IL-6R, wherein the reshaped human L chain V region comprises:

35 (1) FRs of a human L chain V region, and
(2) CDRs of a mouse L chain V region of a monoclonal antibody to the human IL-6R.

44. A DNA coding for a reshaped human L chain

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V region according to claim 43, wherein the CDRs have amino acid sequences shown in any one of SEQ ID NOS: 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

5 45. A DNA coding for a reshaped human L chain
V region according to claim 43, wherein the FRs are
derived from the REI.

46. A DNA according to claim 43, wherein the
L chain V region has an amino acid sequence shown as RV_{La}
or RV_{Lb} in Table 2.

47. A DNA according to claim 43, wherein the L chain V region has an amino acid region shown as RV_L in Table 5.

48. A DNA according to claim 43, having a
nucleotide sequence shown in SEQ ID No: 57.

49. A DNA coding for a reshaped human H chain V region of an antibody to the human IL-6R, wherein the reshaped Human V region comprises:

20 (1) FRs of a human H chain V region, and
(2) CDRs of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

50. A DNA coding for a reshaped human H chain V region according to claim 49, wherein the CDRs have amino acid sequences shown in SEQ ID NOS: 25, 27, 29 and 31 wherein the stretches of the amino acid sequences are defined in Table 9.

51. A DNA coding for a reshaped human H chain V region according to claim 49, wherein the FRs are derived from the NEW or HAX.

30 52. A DNA coding for a reshaped human H chain
V region according to claim 49, wherein the H chain
V region has an amino acid sequence shown as RV_Ha, RV_Hb,
RV_Hc, RV_Hd, RV_He or RV_Hf in Table 3.

53. A DNA according to claim 49, wherein the
H chain V region has an amino acid sequence shown as
RV_Ea, RV_Eb, RV_Ec or RV_Ed in Table 6, or RV_Ha, RV_Hb, RV_Hc or

RV_Ed in Table 7.

54. A DNA according to claim 49, having a nucleotide sequence shown in SEQ ID NO: 56.

5 55. A DNA coding for a reshaped human L chain of an antibody to the human IL-6R, wherein the reshaped human L chain comprises:

10 (1) a human L chain C region; and
(2) an L chain V region comprising a human FRs, and CDRs of a mouse monoclonal antibody to the human IL-6R.

56. A DNA according to claim 55, wherein the L chain V region has the nucleotide sequence shown in SEQ ID NO: 57.

15 57. A DNA coding for a reshaped human H chain of an antibody to the human IL-6R, wherein the reshaped human H chain comprises:

20 (1) a human H chain C region, and
(2) a H chain V region comprising human FRs, and CDRs of a mouse monoclonal antibody to the human IL-6R.

58. A DNA according to claim 57, wherein the H chain V region has the nucleotide sequence shown in SEQ ID NO: 56.

25 59. A vector comprising a DNA according to any one of claims 35, 37, 39, 41, 43, 49, 55 and 57.

60. A host cell transformed or transfected with a vector comprising a DNA according to any one of claims 35, 37, 39, 41, 43, 49, 55 and 57.

30 61. A DNA coding for a chimeric L chain of an antibody to the human IL-6R, wherein the chimeric L chain comprises:

35 (1) a human L chain C region; and
(2) an L chain V region of a mouse monoclonal antibody to the human IL-6R.

62. A DNA coding for a chimeric H chain of an antibody to the human IL-6R wherein the chimeric H chain

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comprises:

- (1) a human H chain C region; and
(2) an H chain V region of a mouse monoclonal antibody to the human IL-6R.

5 63. A process for production of a chimeric antibody
to the human IL-6R, comprising the steps of:

culturing host cells cotransfected with an expression vector comprising a DNA according to claim 61 and with an expression vector comprising a DNA according to claim 62; and

recovering a desired antibody.

64. A process for production of a reshaped human antibody to the human IL-6R, comprising the steps of:

culturing host cells cotransfected with an

15 expression vector comprising a DNA according to claim 55
and with an expression vector comprising a DNA according
to claim 57; and recovering desired antibody.

65. A DNA according to claim 49, having a nucleotide sequence shown in SEQ ID NO: 85, 86 or 94.

20 66. A DNA according to claim 44, having a
nucleotide sequence shown in SEQ IN NO: 71.

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